Alerts, Notices, and Case Reports

Rat-Bite Leptospirosis

JAMES H. GOLLOP, MD, MPH
ALAN R. KATZ,.MD, MPH
RAUL C. RUDOY, MD, MPH
DAVID M. SASAKI, DVM, MPH
Honolulu, Hawaii

LEPTOSPIROSIS, considered the most widespread zoonosis in the world, is transmitted primarily through the direct or indirect exposure of mucous membranes or abraded skin to the urine of an infected animal. Although reported case rates are low in the United States, the protean manifestations and lack of active surveillance frequently lead to missed diagnoses.[1] Leptospirosis has traditionally been classified as an occupational illness of men, with recent trends showing an increasing proportion of exposures through avocational or recreational activities.[2] The ensuing report describes an unusual mode of transmission for leptospirosis, following a rat bite in the home.

Report of a Case

The patient, an 11-year-old Filipino girl, presented to the emergency department of a local hospital because of anorexia, emesis, and myalgias, primarily involving the lower extremities, for four days and fever, severe headache, and neck pain for one day. She had been seen ten days earlier in an outpatient clinic for a rat bite on her left second toe. The treatment included wound dressing with antibiotic ointment and the administration of a tetanus-diphtheria booster. The patient was noted to be residing with her family in an urban low socioeconomic area of Honolulu, Hawaii, in housing with known rat infestation. This was the first episode of a rat bite in the home.

On physical examination in the emergency department, she was thin, alert, oriented, and in mild distress due to neck and head pain. Relevant findings included a temperature of 40.4°C, a pulse rate of 90 beats per minute, a blood pressure of 103/57 mm of mercury, and respirations of 24 per minute. Her neck had a full range of motion although there was subjective pain with motion. Examination of the patient's left second toe revealed a superficial laceration proximal to the nail bed without erythema, edema, or drainage.

Laboratory studies elicited the following values: a peripheral leukocyte count of 5.4×10^9 per liter (0.69 segmented forms, 0.13 band forms, 0.10 lymphocytes, 0.07 monocytes, 0.01 eosinophils), a hematocrit of 0.38 (38%), and a platelet count noted to be adequate. Serum electrolyte analysis was remarkable only for mild hyponatremia (sodium level 128 mmol per liter). A urinalysis revealed a pH of 7 and a specific gravity of 1.018. There was no evidence of proteinuria or bilirubinuria, and microscopic examination showed no abnormalities. A lumbar puncture was done and revealed clear, colorless cerebrospinal fluid (CSF); analysis included a leukocyte count of 12×10^6 per liter (12 per μl) with 0.15 neutrophils, 0.62 lymphocytes, and 0.23 monocytes, and an erythrocyte count of less than 1×10^6 per liter (<1 per μl). The CSF glucose level was 4.2 mmol per liter (75 mg per dl), and the protein level was 0.24 grams per liter (24 mg per dl). Gram's stain examination of both CSF and urine specimens was negative.

The patient was admitted with the presumptive diagnoses of rat-bite fever and aseptic meningitis. The diagnostic evaluation included cultures of blood, urine, and CSF; rapid plasma reagin test; and serologic evaluation for leptospirosis. She was managed with the administration of intravenous penicillin G, 1 million units every four hours, intravenous fluids, and symptomatic treatment of pain and nausea. Her fever subsided, and her neck stiffness abated on the second hospital day. By the third hospital day, her headache had resolved and the patient was asymptomatic. The patient was discharged on the fourth hospital day. Her discharge medications included potassium penicillin V, 2 grams per day by mouth for ten days.

Cultures of blood and CSF specimens obtained on admission showed no growth. Urine culture was positive for *Lactobacillus* species, most likely reflecting vaginal contamination. The rapid plasma reagin test was nonreactive. A serum specimen drawn on hospital day 2 and a specimen drawn three weeks later were tested for antibodies to leptospires at the Centers for Disease Control and Prevention reference laboratory using the microscopic agglutination test. Whereas the specimen drawn during the acute phase was negative, the one taken during the convalescent phase was positive for *Leptospira interrogans,* serovar *mankarso* (serogroup *icterohaemorrhagiae*), with a titer of 1:3,200, confirming the diagnosis of leptospirosis. As part of the case investigation, Hawaii State Department of Health personnel set up rat traps in the home. Of 11 rats (*Rattus norvegicus*) trapped, 3 had kidney cultures positive for *Leptospira* of the same serogroup as found in the case-patient.

Discussion

Leptospirosis is transmitted to humans primarily by direct or indirect contact with the urine of infected animals. Leptospires may enter the body through intact mucous membranes or abraded skin.[3] The domestic rat (*R norvegicus*) may serve as the primary reservoir of leptospirosis in urban areas. At least 78% of rats trapped in

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From the Preventive Medicine Residency Program (Dr Gollop) and Department of Public Health Sciences (Dr Katz), University of Hawaii School of Public Health; Department of Pediatrics (Dr Rudoy), University of Hawaii School of Medicine; and the Communicable Disease Division, Hawaii State Department of Health (Dr Sasaki), Honolulu.

Reprint requests to Alan R. Katz, MD, MPH, Dept of Public Health Sciences, University of Hawaii School of Public Health, 1960 East-West Rd, Honolulu, HI 96822.

urban inner-city Detroit, Michigan, showed serologic evidence of leptospirosis.[4] The six-day time period between the rat bite and the onset of illness corresponds to the usual incubation period for leptospirosis—3 to 10 days.[3] Although transmission associated with animal bites is unusual, cases have been reported with bites from rats,[5-7] a dog,[8] a mouse,[9] and after mouth-to-mouth resuscitation with pigs.[10] Although saliva is not considered an infectious fluid, that from animals in the acute phase of the disease may contain leptospires.[11] Animal-bite–associated transmission has been attributed to either direct inoculation from urine contamination in an animal's mouth or the skin wound serving as a portal of entry for leptospires in the immediate environment.[3]

From 1980 through 1990, the total number of cases reported each year in the United States ranged from only 40 to 100.[12] Surveys of inner-city populations, however, have demonstrated substantial leptospiral seroprevalence rates: 31% of urban youths in Detroit[13] and 16% of inner-city adults in Baltimore, Maryland.[14] Active case finding during a 54-month period in urban St Louis, Missouri, uncovered 9 confirmed and 25 presumptive cases in children.[15] Active surveillance in Hawaii led to a greater than fivefold increase in reported rates.[16]

Subclinical infections are common, and most clinical infections are self-limiting.[3] The most frequently reported symptoms associated with clinical illness are nonspecific and include fever, headache, and myalgias.[1,3] Leptospirosis is most commonly misdiagnosed as aseptic meningitis, fever of unknown origin, or a viral syndrome.[2] The diagnosis may be confirmed by culturing of the organism from blood, CSF, or urine or by demonstrating serologic evidence of infection. The isolation of leptospires from body fluids requires special laboratory techniques, media, and a prolonged incubation time (as long as 6 weeks); hence, serologic testing is the usual means of laboratory confirmation.[3] The Leptospirosis Reference Laboratory of the Centers for Disease Control and Prevention in Atlanta, Georgia, provides serologic diagnostic services and serotyping of positive leptospiral cultures. Physicians desiring this service should contact their respective state health department laboratory or communicable disease unit for advice and assistance in submitting specimens.

Recently conducted double-blind, placebo-controlled trials evaluating the efficacy of antibiotics in the treatment of leptospirosis have shown oral doxycycline, 100 mg twice a day for seven days, to be effective in modifying the disease course in patients with anicteric illness when treatment is initiated within four days of clinical onset.[17] Parenteral penicillin G, 6 million units daily for seven days, showed efficacy in modifying illness in patients with severe icteric disease even when therapy was initiated 7 to 19 days after the symptoms began.[18] Because laboratory confirmation of leptospirosis may take weeks, therapeutic intervention should be instituted as soon as the diagnosis is suspected.

Empiric antibiotic treatment should be considered for any patient presenting with a febrile illness for which there is a history of direct contact with animals or contaminated water or soil within 2 to 26 days of the start of symptoms, especially when symptoms had an abrupt onset and consist of severe headache, chills, myalgias primarily affecting the lower extremities, nausea, and vomiting.[3,19-22] Although conjunctival suffusion has been noted as a pathognomonic feature, it is frequently absent, whereas jaundice occurs in less than 40% of reported cases.[2] For severe cases, parenteral penicillin is considered the drug of choice; less severe cases may be treated with oral tetracycline or doxycycline.[3,20-23] Uncontrolled studies have also reported therapeutic efficacy with ampicillin and amoxicillin.[24]

Because rat infestation is a well-recognized, inner-city housing problem, it is clear that leptospirosis cases from these areas are going unrecognized and hence underreported. Leptospirosis should be included in the differential diagnosis of all patients with rat exposure (including bites) presenting with a febrile illness, as early diagnosis and treatment have been effective in modifying the course of the illness.

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